neovascularization, radiation treatment, transpupillary thermotherapy of subfoveal occult choroidal neovascularization, submacular surgery, limited macular translocation, adjuncts in surgery, argon laser to drusen, infrared diode laser photocoagulation for treatment of wet AMD. Recently, compositions for treating the non-neovascular or dry AMD comprising hypotensive agents, such as hydralazine, were described in U.S. Patent No. 8,088,773 to Chiou, which is incorporated by reference herein.

[0005] The foregoing examples of the related art and limitations related therewith are intended to be illustrative and not exclusive. Other limitations of the related art will become apparent to those of skill in the art upon a reading of the specification and a study of the drawings.

SUMMARY

[0006] The following aspects and embodiments thereof described and illustrated below are meant to be exemplary and illustrative, not limiting in scope.

[0007] Ophthalmic compositions are described. In one embodiment, the ophthalmic composition comprises a pharmaceutically active drug comprising hydralazine in an amount between about 0.02-2 wt%, and one or more of: one or more buffer solutions having a pH of between 3.5-4.5; one or more chelating agents; one or more isotonicity agents; one or more preservatives; one or more viscosity enhancers, and one or more diluents. In an embodiment, the composition has a pH of between 4.0-4.4.

[0007a] In one aspect, there is provided an ophthalmic composition, comprising:

a pharmaceutically active drug comprising hydralazine in an amount between about 0.02-2 wt%;

an acetate buffer solution having pH of between 3.9-4.5 in an amount between 8-12 wt%;

propylene glycol in an amount between 0.5-2 wt%;

sodium chloride in an amount between 0.25-1 wt%;

methylparaben in an amount between 0.015-0.06 wt%;

benzalkonium chloride in the form of a 50% solution, present in an amount between 0.01-0.04 wt%; and

edetate disodium in an amount between 0.008-0.030 wt%;

wherein said composition has a pH of between 4.0-4.4;

wherein a decrease in the wt% of the active drug is less than about 10% after one month storage.

In another embodiment, the ophthalmic composition comprises a pharmaceutically active drug comprising hydralazine in an amount between about 0.02-

IT IS CLAIMED:

1. An ophthalmic composition, comprising:

a pharmaceutically active drug comprising hydralazine in an amount between about 0.02-2 wt%;

an acetate buffer solution having pH of between 3.9-4.5 in an amount between 8-12 wt%;

propylene glycol in an amount between 0.5-2 wt%;

sodium chloride in an amount between 0.25-1 wt%;

methylparaben in an amount between 0.015-0.06 wt%;

benzalkonium chloride in the form of a 50% solution, present in an amount between 0.01-0.04 wt%; and

edetate disodium in an amount between 0.008-0.030 wt%;

wherein said composition has a pH of between 4.0-4.4.

2. The composition of claim 1, wherein the drug is hydralazine hydrochloride.

3. The composition of claim 2, wherein the drug is present in an amount between 0.5-2 wt%.

4. The composition of any one of claims 1-3, wherein the acetate buffer solution has a pH of 4.2 and is present in an amount of 10 wt%.

5. The composition of any one of claims 1-3, wherein the acetate buffer solution is comprised of sodium acetate and 2N acetic acid.

6. The composition of any one of claims 1-5, wherein propylene glycol is present in an amount of 1 wt%.

7. The composition of any one of claims 1-6, wherein methylparaben is present at 0.03 wt%.

8. The composition of any one of claims 1-7, wherein benzalkonium chloride in the form of a 50% solution is present at 0.02 wt%.

9. The composition of any one of claims 1-8, wherein edetate disodium is present

at 0.015 wt%.

10. A method for preparing an ophthalmic formulation, comprising:

mixing water and an acetate buffer solution having a pH 3.9-4.5 to form a first interim mixture, the acetate buffer solution added in an amount to provide between about 8-12 wt% of acetate buffer solution in the formulation;

adding to the first interim mixture edetate disodium, to form a second interim mixture, the edetate disodium added in an amount to provide between about 0.008-0.030 wt% of edetate disodium in the formulation;

adding to the second interim mixture propylene glycol to form a third interim mixture, the propylene glycol added in an amount to provide between about 0.5-2 wt% of propylene glycol in the formulation;

adding to the third interim mixture sodium chloride to form a fourth interim mixture, the sodium chloride added in an amount to provide between about 0.25-1 wt% of sodium chloride in the formulation;

adding to the fourth interim mixture benzalkonium chloride to form a fifth interim mixture, the benzalkonium chloride added in an amount to provide between about 0.01-0.04 wt% of benzalkonium chloride in the formulation; and

adding to the fifth interim mixture methylparaben to form a sixth interim mixture, the methylparaben added in an amount to provide between about 0.015-0.06 wt% of methylparaben in the formulation;

adding to the sixth interim mixture to form said formulation, a pharmaceutically active drug comprising hydralazine.

11. The method of claim 10, wherein one or more of the steps of adding comprise mixing while adding.

12. The method of any one of claims 10-11, wherein the acetate buffer solution is added in an amount to provide 10 wt% acetate buffer in the formulation.

13. The method of any one of claims 10-12, wherein the acetate buffer solution is comprised of sodium acetate and 2N acetic acid.

14. The method of any one of claims 10-13, wherein edetate disodium is added in an amount to provide 0.015 wt% edetate disodium in the formulation.

15. The method of any one of claims 10-14, wherein propylene glycol is added in an amount to provide 15 wt% propylene glycol in the formulation.

16. The method of any one of claims 10-15, wherein sodium chloride is added in an amount to provide 0.5 wt% sodium chloride in the formulation.

17. The method of any one of claims 10-16, wherein benzalkonium chloride is added in an amount to provide 0.02 wt% benzalkonium chloride in the formulation.

18. The method of any one of claims 10-17 wherein methylparaben is added in an amount to provide 0.03 wt% methylparaben in the formulation.

19. The method of any one of claims 10-18, wherein the pharmaceutically active drug is hydralazine present in the formulation at between 0.5-2 wt%.

20. The ophthalmic composition of any one of claims 1-9 for use in treating macular degeneration.

21. The composition of claim 20, wherein said macular degeneration is dry age-related macular degeneration.

22. Use of the ophthalmic composition of any one of claims 1-9 or the formulation prepared according to the method of any one of claims 10-19 in the manufacture of a medicament for treating macular degeneration, wherein said medicament is to be administered to an eye of a subject at risk of or diagnosed with macular degeneration.

23. The use of claim 22, wherein said macular degeneration is age-related dry macular degeneration.

IT IS CLAIMED:

1. An ophthalmic composition, comprising:

a pharmaceutically active drug comprising hydralazine in an amount between about 0.02-2 wt%;

an acetate buffer solution having pH of between 3.9-4.5 in an amount between 8-12 wt%;

propylene glycol in an amount between 0.5-2 wt%;

sodium chloride in an amount between 0.25-1 wt%;

methylparaben in an amount between 0.015-0.06 wt%;

benzalkonium chloride in the form of a 50% solution, present in an amount between 0.01-0.04 wt%; and

edetate disodium in an amount between 0.008-0.030 wt%;

wherein said composition has a pH of between 4.0-4.4;

wherein a decrease in the wt% of the active drug is less than about 10% after one month storage.

2. The composition of claim 1, wherein the drug is hydralazine hydrochloride.

3. The composition of claim 2, wherein the drug is present in an amount between 0.5-2 wt%.

4. The composition of any one of claims 1-3, wherein the acetate buffer solution has a pH of 4.2 and is present in an amount of 10 wt%.

5. The composition of any one of claims 1-3, wherein the acetate buffer solution is comprised of sodium acetate and 2N acetic acid.

6. The composition of any one of claims 1-5, wherein propylene glycol is present in an amount of 1 wt%.

7. The composition of any one of claims 1-6, wherein methylparaben is present at 0.03 wt%.

8. The composition of any one of claims 1-7, wherein benzalkonium chloride in the

form of a 50% solution is present at 0.02 wt%.

9. The composition of any one of claims 1-8, wherein edetate disodium is present at 0.015 wt%.

10. A method for preparing an ophthalmic formulation, comprising:

mixing water and an acetate buffer solution having a pH 3.9-4.5 to form a first interim mixture, the acetate buffer solution added in an amount to provide between about 8-12 wt% of acetate buffer solution in the formulation;

adding to the first interim mixture edetate disodium, to form a second interim mixture, the edetate disodium added in an amount to provide between about 0.008-0.030 wt% of edetate disodium in the formulation;

adding to the second interim mixture propylene glycol to form a third interim mixture, the propylene glycol added in an amount to provide between about 0.5-2 wt% of propylene glycol in the formulation;

adding to the third interim mixture sodium chloride to form a fourth interim mixture, the sodium chloride added in an amount to provide between about 0.25-1 wt% of sodium chloride in the formulation;

adding to the fourth interim mixture benzalkonium chloride to form a fifth interim mixture, the benzalkonium chloride added in an amount to provide between about 0.01-0.04 wt% of benzalkonium chloride in the formulation; and

adding to the fifth interim mixture methylparaben to form a sixth interim mixture, the methylparaben added in an amount to provide between about 0.015-0.06 wt% of methylparaben in the formulation;

adding to the sixth interim mixture to form said formulation, a pharmaceutically active drug comprising hydralazine.

11. The method of claim 10, wherein one or more of the steps of adding comprise mixing while adding.

12. The method of any one of claims 10-11, wherein the acetate buffer solution is added in an amount to provide 10 wt% acetate buffer in the formulation.

13. The method of any one of claims 10-12, wherein the acetate buffer solution is comprised of sodium acetate and 2N acetic acid.

14. The method of any one of claims 10-13, wherein edetate disodium is added in an amount to provide 0.015 wt% edetate disodium in the formulation.

15. The method of any one of claims 10-14, wherein propylene glycol is added in an amount to provide 1 wt% propylene glycol in the formulation.

16. The method of any one of claims 10-15, wherein sodium chloride is added in an amount to provide 0.5 wt% sodium chloride in the formulation.

17. The method of any one of claims 10-16, wherein benzalkonium chloride is added in an amount to provide 0.02 wt% benzalkonium chloride in the formulation.

18. The method of any one of claims 10-17, wherein methylparaben is added in an amount to provide 0.03 wt% methylparaben in the formulation.

19. The method of any one of claims 10-18, wherein the pharmaceutically active drug is hydralazine present in the formulation at between 0.5-2 wt%.

20. The ophthalmic composition of any one of claims 1-9 for use in treating macular degeneration.

21. The composition of claim 20, wherein said macular degeneration is dry age-related macular degeneration.

22. Use of the ophthalmic composition of any one of claims 1-9 or the formulation prepared according to the method of any one of claims 10-19 in the manufacture of a medicament for treating macular degeneration, wherein said medicament is to be administered to an eye of a subject at risk of or diagnosed with macular degeneration.

23. The use of claim 22, wherein said macular degeneration is age-related dry macular degeneration.

24. The composition of claim 1, wherein a decrease in the wt% of the active drug is

less than about 1.0% after one month storage.

25. The composition of claim 1, wherein a decrease in the wt% of the active drug is less than about 0.5% after one month storage.

26. The composition of claim 1, wherein the composition is stored at about 25°C.

27. The composition of claim 1, wherein the composition is stored at about 40°C.